

What is claimed is:

1. A method for preventing or treating diabetes in a mammal, the method comprising administering to the mammal a therapeutically effective amount of at least one GLP-1 or a related molecule having GLP-1, wherein the amount and timing of administration are
5 such as to prevent or treat diabetes in the mammal without the continuous presence of the molecule.
2. The method of claim 1, wherein the method further comprises reducing administration of the GLP-1 or related molecule below about the therapeutically effective amount for a time conducive to producing a drug holiday, the method being sufficient to prevent or
10 treat the diabetes or related disorder in the mammal.
3. The method of claim 2, wherein administration of the GLP-1 or related molecule is reduced during the drug holiday by at least about 50% below the therapeutic amount.
4. The method of claim 3, wherein administration of the GLP-1 or related molecule is reduced during the drug holiday by at least about 90% below the therapeutic amount.
- 15 5. The method of claim 4, wherein administration of the GLP-1 or related molecule is stopped during the drug holiday.
6. The method of claims 1-5, wherein during the drug holiday is further defined as a time interval between a first endpoint following the reduction in administering the GLP-1 or related molecule and a second endpoint.
- 20 7. The method of claim 6, wherein the second endpoint is identified by a standard FBG or glycosylated hemoglobin test.
8. The method of claims 1-7, wherein the drug holiday is for about one day to about twenty five weeks.

9. The method of claim 8, wherein the drug holiday is for between from about three to four weeks.
10. The method of claims 1-9, wherein the GLP-1 or related molecule is administered as a depot formulation.
- 5 11. The method of claims 1-10, wherein the GLP-1 or related molecule is administered to the mammal bolus at least about once daily.
12. The method of claim 11, wherein the GLP-1 or related molecule is administered to the mammal bolus at least once a week.
- 10 13. The method of claims 1-12, wherein the administration of the GLP-1 or related molecule is about twice daily (i.v. or subQ) for between from about one to about twenty weeks.
14. The method of the claim 1, wherein the method further comprises administering to the mammal a second therapeutically effective amount of GLP-1 or a related molecule following the drug holiday.
- 15 15. The method of claim 14, wherein the method further comprises reducing administration of the second therapeutically effective amount of GLP-1 or related molecule for a time conducive to producing a second drug holiday.
16. The method of claim 1 or 15, wherein the administration and reducing steps are repeated at least once.
- 20 17. The method of claim 16, wherein the administration and reducing steps are repeated at least about 2 to about 25 times.
18. The method of claim 17, wherein the administration and reducing steps are repeated as needed to prevent or treat the diabetes or related disorder.

19. The method of claim 18, wherein the method is practiced over the lifetime of the mammal.
20. The method of claims 1-19, wherein the GLP-1 or related molecule is administered to the mammal at a dose of at least about 0.01 nmol/kg (body weight).
- 5 21. The method of claims 1-20, wherein the GLP-1 or related molecule has been disclosed in U.S. Pat. Nos. 6,358,924; 6,344,180; 6,284,725; 6,277,819; 6,271,241; 6,268,343; 6,191,102; 6,051,689; 6,006,753; 5,846,937; 5,670,360; 5,614,492; 5,846,937; 5,545,618; 6,410,508; 6,388,053; 6,384,016; 6,329,336; 6,110,703; 5,846,747; 5,670,360; or 5,631,224.
- 10 22. The method of claims 1-21, wherein the GLP-1 or related molecule is exendin-4, exendin-3; or an analog or derivative thereof.
23. The method of claim 22, wherein the exendin-4, exendin-3; or derivative thereof has been disclosed in U.S. Patent No. 5,424,286; WO98/05351; WO98/30231; WO99/07404, WO 99/25727; WO 99/25728; WO 99/46283; PCT/DK00/00393; or published EP
- 15 Application No. 99610043.4.
24. The method of claims 1-23, wherein the method further comprises administering at least one anti-diabetic drug to the mammal.
25. The method of claim 24, wherein the administration is below about a therapeutically effective amount for at least one of the drugs in the mammal.
- 20 26. The method of claim 24, wherein the administration is at least about a therapeutically effective amount for at least one of the drugs in the mammal.
27. The method of claims 1-26, wherein administration of the anti-diabetic drug is before or after the drug holiday.

28. The method of claims 1-27, wherein at least one of the anti-diabetic drugs is insulin, an insulin analog; or a pharmaceutically acceptable mixture thereof.

29. The method of claim 28, wherein the insulin is human insulin, bovine insulin, porcine insulin; or a mixture thereof.

5 30. The method of claims 1-29, wherein the insulin analog is Lys (B28), Pro (B29) human insulin.

31. The method of claims 1-30, wherein the anti-diabetic drug is a sulfonylurea, biguanide, thiazolidinedione, diazoxide, somatostatin, or an alpha-glucosidase inhibitor.

10 32. The method of claim 31, wherein the sulfonylurea is selected from the group consisting of tolbutamide, chlorpropamide, tolazamide, acetohexamide, glyburide, glipizide, and gliclazide.

33. The method of claim 31, wherein the biguanide is metformin or phenformin.

34. The method of claim 31, wherein the thiazolidinedione is ciglitazone or pioglitazone.

15 35. The method of claim 31, wherein the alpha-glucosidase inhibitor is acarbose.

36. The method of claims 1-35, wherein the mammal is a human subject who has or is suspected of having diabetes mellitus or a related disorder.

20 37. The method of claim 36, wherein the diabetes mellitus is selected from the group consisting of insulin-dependent diabetes mellitus (IDDM or type I diabetes) and non-insulin-dependent diabetes mellitus (NIDDM, or type II diabetes).

38. The method of claim 36, wherein the human subject suspected of having the diabetes mellitus is genetically pre-disposed to develop the disease.

39. The method of claim 36, wherein the disorder related to diabetes mellitus is selected from the group consisting of impaired glucose tolerance (IGT), maturity-onset diabetes of youth (MODY); leprechaunism (insulin receptor mutation), tropical diabetes, diabetes secondary to a pancreatic disease or surgery; diabetes associated with a genetic syndrome (eg., Prader-Willi syndrome); pancreatitis; and diabetes secondary to endocrinopathies; adipositas; and metabolic syndrome (syndroma X).
40. Use of at least one GLP-1 or a related molecule having GLP-1 effect for the manufacture of a medicament for preventing or treating diabetes in a mammal, wherein the amount and timing of administration of said medicament are such as to prevent or treat diabetes in the mammal without the continuous presence of said molecule.
41. The use according to claim 40, further comprising reducing administration of the GLP-1 or related molecule below about the therapeutically effective amount for a time conducive to producing a drug holiday.
42. The use according to claim 41, wherein administration of the GLP-1 or related molecule is reduced during the drug holiday by at least about 50% below the therapeutic amount.
43. The use according to claim 42, wherein administration of the GLP-1 or related molecule is reduced during the drug holiday by at least about 90% below the therapeutic amount.
44. The use according to claim 43, wherein administration of the GLP-1 or related molecule is stopped during the drug holiday.
45. The use according to claims 40-44, wherein during the drug holiday is further defined as a time interval between a first endpoint following the reduction in administering the GLP-1 or related molecule and a second endpoint.

46. The use according to claim 45, wherein the second endpoint is identified by a standard FBG or glycosylated hemoglobin test.

47. The use according to claims 40-46, wherein the drug holiday is for about one day to about twenty-five weeks.

5 48. The use according to claim 47, wherein the drug holiday is for between from about three to four weeks.

49. The use according to claims 40-48, wherein the GLP-1 or related molecule is administered as a depot formulation.

10 50. The use according to claims 40-49, wherein the GLP-1 or related molecule is administered to the mammal bolus at least about once daily.

51. The use according to claim 50, wherein the GLP-1 or related molecule is administered to the mammal bolus at least once a week.

15 52. The use according to claims 40-51, wherein the administration of the GLP-1 or related molecule is about twice daily (i.v. or subQ) for between from about one to about twenty weeks.

53. The use according to claim 40, further comprising administering to the mammal a second therapeutically effective amount of GLP-1 or a related molecule following the drug holiday.

20 54. The use according to claim 53, further comprising reducing administration of the second therapeutically effective amount of GLP-1 or related molecule for a time conducive to producing a second drug holiday.

55. The use according to claim 40 or 54, wherein the administration and reducing steps are repeated at least once.

56. The use according to claim 55, wherein the administration and reducing steps are repeated at least about 2 to about 25 times.

57. The method of claim 56, wherein the administration and reducing steps are repeated as needed to prevent or treat the diabetes or related disorder.

5 58. The use according to claim 57, wherein the use is practiced over the lifetime of the mammal.

59. The use according to claims 40-58, wherein the GLP-1 or related molecule is administered to the mammal at a dose of at least about 0.01 nmol/kg (body weight).

10 60. The use according to claims 40-59, wherein the GLP-1 or related molecule has been disclosed in U.S. Pat. Nos. 6,358,924; 6,344,180; 6,284,725; 6,277,819; 6,271,241; 6,268,343; 6,191,102; 6,051,689; 6,006,753; 5,846,937; 5,670,360; 5,614,492; 5,846,937; 5,545,618; 6,410,508; 6,388,053; 6,384,016; 6,329,336; 6,110,703; 5,846,747; 5,670,360; or 5,631,224.

15 61. The use according to claims 40-62, wherein the GLP-1 or related molecule is exendin-4, exendin-3; or an analog or derivative thereof.

62. The use according to claim 61, wherein the exendin-4, exendin-3; or derivative thereof has been disclosed in U.S. Patent No. 5,424,286; WO98/05351; WO98/30231; WO99/07404, WO 99/25727; WO 99/25728; WO 99/46283; PCT/DK00/00393; or published EP Application No. 99610043.4.

20 63. The use according to claims 40-62, wherein the method further comprises administering at least one anti-diabetic drug to the mammal.

64. The use according to claim 63, wherein the administration is below about a therapeutically effective amount for at least one of the drugs in the mammal.

65. The use according to claim 63, wherein the administration is at least about at a therapeutically effective amount for at least one of the drugs in the mammal.

66. The use according to claims 40-65, wherein administration of the anti-diabetic drug is before or after the drug holiday.

5 67. The use according to claims 40-66, wherein at least one of the anti-diabetic drugs is insulin, an insulin analog; or a pharmaceutically acceptable mixture thereof.

68. The use according to claim 67, wherein the insulin is human insulin, bovine insulin, porcine insulin; or a mixture thereof.

10 69. The use according to claims 40-68, wherein the insulin analog is Lys (B28), Pro (B29) human insulin.

70. The use according to claims 40-69, wherein the anti-diabetic drug is a sulfonylurea, biguanide, thiazolidinedione, diazoxide, somatostatin, or an alpha-glucosidase inhibitor.

15 71. The use according to claim 70, wherein the sulfonylurea is selected from the group consisting of tolbutamide, chlorpropamide, tolazamide, acetohexamide, glyburide, glipizide, and gliclazide.

72. The use according to claim 70, wherein the biguanide is metformin or phenformin.

73. The use according to claim 70, wherein the thiazolidinedione is ciglitazone or pioglitazone.

74. The use according to claim 70, wherein the alpha-glucosidase inhibitor is acarbose.

20 75. The use according to claims 40-74, wherein the mammal is a human subject who has or is suspected of having diabetes mellitus or a related disorder.

76. The use according to claim 75, wherein the diabetes mellitus is selected from the group consisting of insulin-dependent diabetes mellitus (IDDM or type I diabetes) and non-insulin-dependent diabetes mellitus (NIDDM, or type II diabetes).

5 77. The use according to claim 75, wherein the human subject suspected of having the diabetes mellitus is genetically pre-disposed to develop the disease.

78. The use according to claim 75, wherein the disorder related to diabetes mellitus is selected from the group consisting of impaired glucose tolerance (IGT), maturity-onset diabetes of youth (MODY); leprechaunism (insulin receptor mutation), tropical diabetes, diabetes secondary to a pancreatic disease or surgery; diabetes associated with a genetic syndrome (eg., Prader-Willi syndrome); pancreatitis; and diabetes secondary to
10 endocrinopathies; adipositas; and metabolic syndrome (syndroma X).